

# Preparation of some New Derivatives of 5,6-Diphenyl-1,2,4-triazine-3-hydrazines and their Biological Evaluation

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Some new derivatives of 5,6-diphenyl-1,2,4-triazine-3-hydrazines (3a-p) were prepared by the condensation of 5,6-diphenyl-1,2,4-triazine-3-hydrazine (2) with substituted-aldehydes, acetophenones, isatins and phenyl isothiocyanates. The condensation products were screened for their antiviral activity

**TRIAZINES** exhibit various biological activities<sup>1</sup>. Hydrazones, thiosemicarbazones and Schiff bases also exhibit diverse biological actions. In addition, notable pesticidal activity of indoline-2,3-dione has long been established<sup>2</sup>. Keeping these in view it was thought of interest to prepare various condensation products of substituted-triazine-3-hydrazine (2) and study their antiviral action.

5,6-Diphenyl-1,2,4-triazine-3-thiol (1) was obtained by reacting thiosemicarbazide with benzil in presence of aqueous potassium carbonate. The thiol group was then replaced by the hydrazine

group by refluxing 1 with excess hydrazine hydrate for 8-10 h when 5,6-diphenyl-1,2,4-triazine-3-hydrazine (2) was obtained. Treatment of 2 with various aldehydes resulted in the Schiff bases (3a-g). 2 when condensed with different ketones and 1H-5-substituted indoline-2,3-diones yielded the hydrazones (3h-n). 2 when treated with 4-substituted phenyl isothiocyanate gave the thiosemicarbazones (3o-p; Scheme 1).

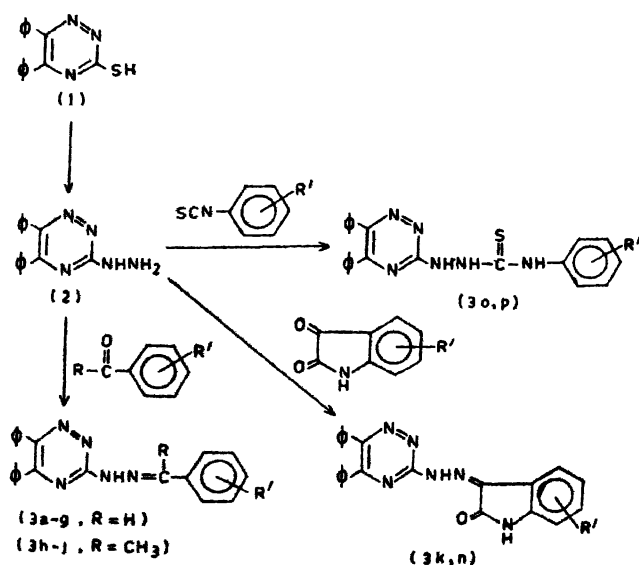
The structures of these compounds were established by elemental and spectral data. The appearance of ir bands at 3300 (NH) and 1600  $\text{cm}^{-1}$  (C=N) confirmed the structure of the titled compounds.

## Experimental

Melting points were taken in open capillary tubes in an electrical melting point apparatus and are uncorrected. Ir spectra (KBr) were recorded on a Perkin-Elmer 177 spectrophotometer. The purity of compounds were checked by tlc on silica gel G plates and spots were visualised by iodine vapours.

**5,6-Diphenyl-1,2,4-triazine-3-thiol (1)**: It was prepared by the reported method<sup>3</sup>.

**5,6-Diphenyl-1,2,4-triazine-3-hydrazine 2**: 1 (1 mol) was refluxed with an excess of hydrazine hydrate<sup>4</sup> for 8-10 h. Hydrazine hydrate was then removed under reduced pressure and the resulting solid was washed with ethanol and crystallised from ethanol, (60%), m.p. 145° (Found: C, 67.9; H, 4.2; N, 25.3.  $\text{C}_{18}\text{H}_{13}\text{N}_5$  requires: C, 68.4; H, 4.9; N, 26.6%).



Scheme 1

**1-(5,6-Diphenyl-1,2,4-triazine)-2-(arylidene)hydrazones (3a–g) :** To a solution of the hydrazine (2; 0.001 mol in 50 ml ethanol) were added various substituted aromatic aldehydes (0.001 mol) and glacial acetic acid (2 drops) and the contents refluxed for 4 h. It was then concentrated and cooled and the resulting solid was washed with alcohol, dried and crystallised from dimethyl formamide (Table 1): **3a** (71%), m.p. 258° (Found: C, 68.2; H, 4.3; N, 18.5.  $C_{22}H_{16}H_5Cl$  requires: C, 68.5; H, 4.2; N, 18.2%);  $\nu_{max}$  (KBr), 1 620 (C=N), 2 900 (NH) and 2 400  $cm^{-1}$  (CH).

**1-(4'-Substituted-acetophenone)-5,6-diphenyl-1,2,4-triazine-3-yl-hydrazones (3h–j) :** To a solution of 2 (0.01 mol) in methanol (50 ml) were added various substituted-ketones (0.01 mol) and glacial acetic acid (1–2 drops). The reaction mixture was refluxed for 5–6 h. It was then concentrated and cooled, and the resulting solid was dried and crystallised from dimethyl formamide (Table 1): **3h** (68%), m.p. 262° (Found: C, 68.5; H, 4.0; N, 17.0.  $C_{23}H_{18}N_6Cl$  requires: C, 69.1; H, 4.5; N, 17.5%);  $\nu_{max}$  (KBr) 1 615 (C=N), 2 900 (NH) and 2 400  $cm^{-1}$  (CH); **3i**  $\delta$  2.2 (3H, s,  $CH_3$ ), 3.5 (1H, s, NH), 7.5 (14H, m, ArH) and 9.7 (1H, s, OH).

**5-Substituted-indoline-2,3-diones :** The compounds were prepared according to the reported methods<sup>8</sup>.

TABLE 1 – PHYSICAL DATA OF COMPOUNDS 3

Compd. no.	R	R'	M.p. °C	Yield %	Mol. formula
3a	H	4-Cl	258	71	$C_{22}H_{16}N_6Cl$
3b	H	4-OCH <sub>3</sub>	245	72	$C_{23}H_{18}N_6O$
3c	H	4-OH	229	65	$C_{22}H_{17}N_6O$
3d	H	H	210	65	$C_{22}H_{17}N_6$
3e	H	2,4-(OCH <sub>3</sub> ) <sub>2</sub>	232	60	$C_{24}H_{20}N_6O_2$
3f	H	2-OH	255	70	$C_{23}H_{17}N_6O$
3g	H	4-N(CH <sub>3</sub> )	248	70	$C_{23}H_{19}N_6$
3h	CH <sub>3</sub>	4-Cl	262	68	$C_{23}H_{18}N_6Cl$
3i	CH <sub>3</sub>	4-OH	256	66	$C_{23}H_{18}N_6O$
3j	CH <sub>3</sub>	H	260	69	$C_{23}H_{19}N_6$
3k	–	H	288	72	$C_{22}H_{16}N_6O$
3l	–	5-CH <sub>3</sub>	283	70	$C_{23}H_{18}N_6O$
3m	–	5-Cl	283	75	$C_{23}H_{16}N_6OCl$
3n	–	5-Br	285	72	$C_{23}H_{16}N_6OBr$
3o	–	4-Cl	242	55	$C_{23}H_{17}N_6ClS$
3p	–	4-CH <sub>3</sub>	232	58	$C_{24}H_{20}N_6S$

\*All compounds gave satisfactory C, H and N analyses.

**5,6-Diphenyl-3-hydrazono-3'-(5-substituted-indolin-2-one)triazines (3k–n) :** To a solution of 2 (0.01 mol) in alcohol were added 1H-5-substituted-indoline-2,3-dione (0.01 mol) and glacial acetic acid (2–3 drops). The reaction mixture was refluxed for 5 h. It was then concentrated and

cooled and the resulting solid was washed with alcohol, dried and crystallised from dimethyl formamide (Table 1): **3l** (70%), m.p. 283° (Found: C, 70.2; H, 5.0; N, 19.8.  $C_{24}H_{18}N_6O$  requires: C, 70.9; H, 4.4; N, 20.7%);  $\nu_{max}$  (KBr) 1 740 (C=O), 1 610 (C=N), 3 300 (NH of indolinone) and 2 900  $cm^{-1}$  (NH).

**Aryl isothiocyanates :** The compounds were prepared by reported methods<sup>9</sup>.

**N-Aryl-2-(5,6-diphenyl-1,2,4-triazino-3-yl)hydrazine carbothioamide (3o–p) :** A mixture of a solution of 2 (0.005 mol) in alcohol (25 ml) and various aryl isothiocyanates (0.005 mol) was refluxed for 4–5 h. It was then concentrated and cooled and the resulting solid was washed with cold alcohol, dried and crystallised from aqueous DMF (Table 1): **3o** (55%), m.p. 242° (Found: C, 60.5; H, 4.2; N, 19.2.  $C_{23}H_{17}N_6ClS$  requires: C, 61.0; H, 3.9; N, 19.4%);  $\nu_{max}$  3 320 (NH), 2 950 (CH), 1 620 (C=N), 1 230 and 1 255  $cm^{-1}$  (C=S, C–S).

**Biological activity :** In this series 14 compounds were screened for their antiviral activity. Sunhemp Rosette virus (SRV-strain of TMV) maintained on host cyanopsis tetragonoloba plants, and against cucumber green mottle mosaic virus (CGMMV) maintained on host chenopodium amaranti colour. The reported procedure<sup>7</sup> was followed for *in vitro* and *in vivo* antiviral testing. The test solutions of the compounds were prepared by dissolving the sample (5 mg) in DMF (1 ml) and making the volume to 5 ml with distilled water.

## Results and Discussion

All the compounds inhibited the viral growth in a range of 22–53% *in vivo*, 18–63% *in vitro* against SRV and 20–48% *in vitro*, 19–67% *in vivo* against CGMMV. Few compounds (**3c**, **d**, **f**, **k** and **n**) caused good inhibition against SRV while compounds **3c–e** showed moderate inhibition against CGMMV. So the details of biological activity are not reported.

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